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(54) Reference electrode consisting of insulated-gate field-effect transistor

(57) A reference electrode for use in systems for selective detection and measurement of chemical properties of substances consisting of an insulated-gate field-effect transistor in which the surface of the gate region is coated with a hydrophobic organic polymer membrane. The reference electrode and a chemical sensitive IGFET can be formed in a common silicon body and share a common drain region. A wide range of suitable hydrophobic materials and methods of forming the membrane are described.

## SPECIFICATION

## Reference electrode of insulated-gate field-effect transistor

- 5 This invention relates to a reference electrode of an insulated-gate field-effect transistor (hereinafter referred to as "FET") and also to a system for selective detection and measurement of chemical properties of substances using this reference electrode. The term "chemical properties" is used in this invention to include the activity and concentration of ions, the presence and concentration of enzymes, substrates, antibodies, antigens, hormones and
- 10 reducible gases and the presence, concentration and activity of various chemical substances and biochemical substances. More particularly, but not exclusively, the invention is concerned with the selective detection and measurement of the activity and concentration of ions.
- Glass electrodes have hitherto been used for selective measurement of quantities of chemical substances in samples. Electrodes of this type are valuable for selective determination of
- 15 activities of chemical substances, especially various ions in the living body, in the medical and physiological fields. In these conventional electrodes, however, since the resistance of the glass film is about 10 megohms, a high-input resistance amplifier is required. Further, the glass film is thin and has poor mechanical strength. Moreover, when the quantity of a specific chemical substance existing in a location of very small volume is to be measured, the need for having
- 20 only a small area of contact between the glass electrode and the substance means that the resistance of the glass film is especially increased. Accordingly, it is difficult to insulate portions other than the top end in the electrode. Therefore, when an electrode of this type is used, it is technically difficult to measure the quantity of a specific chemical substance in a location of small volume.
- 25 Recently, a novel small sensor, in which the foregoing defects of glass electrodes are eliminated, was proposed by K D Wise et al. in IEEE, Trans. on BME, Vol. BME-21, No. 6, pp. 485-487, 1974. According to this proposal, a gate-insulated FET is used, in which silicon nitride, which is excellent in water resistance, is further coated on the surface of an insulated gate layer composed of silicon dioxide, and the precision of measurement in aqueous solutions
- 30 is improved by adoption of this structure. Such an FET can be used as a sensor sensitive to the hydrogen ion. In the above report, K D Wise et al. suggested that an FET having the above structure would possibly be a sensor capable of selectively detecting various chemical substances. Further, the structure of an FET that can selectively detect and measure various chemical properties is disclosed in U.S. Patent No. 4,020,830. The disclosed sensor has an
- 35 insulated gate layer composed of silicon dioxide or silicon nitride and a layer having a chemical selectivity, such as used in a glass electrode, coated on the surface of the insulated gate layer. By utilizing this sensor, such ions as sodium ions and potassium ions can be measured.
- Still further, Published Japanese Patent Application No. 26292/77 discloses an FET sensor comprising an insulated gate layer composed of silicon dioxide, silicon nitride and a top coating
- 40 selectively sensitive to specific chemical substances.
- In the above-mentioned FET sensor, the size can be decreased and the defect inherently involved in a glass electrode, namely a high electrode resistance, be eliminated. Therefore, this sensor can be advantageously used as a miniature electrode, especially in the medical and biological fields. When such a sensor is used, however, it is essential to use a reference
- 45 electrode providing a certain potential difference irrespective of the ion concentration in the liquid being tested.
- Electrodes dipped in an internal reference solution, such as a calomel electrode, a silver chloride electrode and a mercuric oxide electrode, have hitherto been used as reference electrodes, and electrodes of this type are also disclosed in U.S. Patent No. 4,020,830. In such
- 50 reference electrodes, an internal reference liquid should be contacted with the solution to be tested through a liquid junction. These reference electrodes are divided into three types, namely the pinhole type, the sleeve type and the fibre type according to the structure of the liquid junction. In each type, if the size of the liquid junction is diminished in order to prevent the internal reference solution from flowing out, measurement values become unstable, because of
- 55 the increase in resistance. Accordingly, the liquid junction must be at least a certain size, and hence the internal reference solution cannot be prevented from flowing out of the liquid junction. Therefore, if outflow of the internal reference solution is taken into account, the quantity of the internal reference solution and hence the size of the reference electrode cannot be reduced below a certain level. Therefore, even if a very small FET sensor is used, the
- 60 reference electrode used in combination will be too large to enable a minute substance to be measured and measurement will be impossible in a small vessel. For this reason, it has been desired to develop a small reference electrode capable of allowing an FET to exert its characteristics sufficiently.

Recently, several reference electrodes have been proposed with the aim of meeting this

J. Janata proposed a reference electrode in which an FET sensor is dipped in an internal reference solution, instead of the silver chloride electrode customarily used as a reference electrode, and is put in contact with the liquid to be tested through a liquid junction. In this proposal, since an FET is used instead of the conventional reference electrode, the size can be decreased to some extent, but since an internal reference solution is used, decrease of the size is inevitably limited. Further, it is very difficult to manufacture a minute electrode having such a structure. Separately, Japanese Published Patent Application No. 26292/77 discloses the use as a reference electrode of an FET sensitive to a substance of a constant concentration in a liquid to be tested. As one example of such means, there is proposed a reference electrode comprising silver-plus-silver-chloride coated on the surface of a gate region of an FET. This electrode acts as a sensor selectively detecting the concentration of chlorine ions. Accordingly, this electrode can be used as a reference electrode in the tissue of a living body where the chloride ion concentration is constant. This electrode, however is defective in that since the potential is charged according to the chlorine ion concentration, it has only limited uses.

In accordance with the present invention, there is provided a reference electrode comprising an insulated gate field effect transistor in which the surface of the gate region is coated with a hydrophobic and non-ionic organic polymeric membrane. The electrode of the present invention is not sensitive to chemical properties but is selectively sensitive to the potential of a liquid to be tested. It is also much smaller than convention electrodes and can be used in certain systems for measurement of chemical properties in a liquid that have a much diminished size and are effective for detecting and measuring various ion concentrations in a living body.

The present invention thus also provides a system for measuring chemical properties comprising a chemical-property-measuring unit including an insulated-gate field-effect transistor that is sensitive to chemical properties in a liquid to be tested; a reference electrode comprising an insulated gate field effect transistor, the surface of the gate region of which is coated with a hydrophobic organic polymeric membrane so that the transistor is not sensitive to chemical properties in the liquid to be tested; and a pseudo reference electrode comprising an electrode formed of a good electric conductor. This system can be an integrated composite measurement system in which the unit for measurement of chemical properties and the reference electrode are integrally built.

The reference electrode of this invention can be constructed by using a known insulated gate FET. Such known insulated gate FETs are disclosed, for example, in the paper by K D Weise et al, in U.S. Patent No. 4,020,830 and in Japanese Published Patent Application No. 26292/77. The gate-insulating layer of the FET is ordinarily composed of silicon dioxide or silicon nitride. A gate-insulating layer having a two-layer structure comprising a silicon dioxide layer on which a silicon nitride layer is formed is especially preferred.

The reference electrode of the present invention is manufactured by coating the gate-insulating layer with the hydrophobic organic polymeric membrane. In the case where the surface of an insulated gate is composed of an oxide or nitride, an interfacial potential is considered to be generated, e.g. by hydrogen ions, according to the dissociation equilibrium of hydroxyl groups on the surface. In contrast, if the surface is coated with a hydrophobic organic polymer membrane free of an ionic dissociative group, the liquid to be tested is not allowed to come into contact with the gate surface so that no interfacial potential is generated and therefore the electrode can be effectively used as a reference electrode.

Thus, as will be apparent from the foregoing illustration an organic polymer membrane to be formed on the gate surface in accordance with this invention should be so water-impermeable that the gate surface is prevented from coming into contact with the liquid being tested. Hydrophobic membranes are ordinarily water-impermeable. In this specification the term "hydrophobic membrane" means a membrane in which the water content, determined with respect to a membrane formed under the same conditions as the membrane to be coated on a gate region, according to the method of ASTM D570-63, is lower than 0.5% by weight. As is illustrated in the Examples given hereinafter, an electrode provided with such membrane is not sensitive to ions in a liquid to be tested.

U.S. Patent No. 4,020,830 mentioned above discloses a sensor comprising an insulated gate FET coated with a hydrophobic membrane. However, the disclosed hydrophobic membrane necessarily contains a ligand capable of selectively adsorbing specific substances and rendering the gate surface sensitive to chemical properties. Accordingly, an electrode coated with such a membrane can be used as a sensor but cannot be used as a reference electrode. The hydrophobic organic polymer membrane used in accordance with this invention does not contain such a ligand at all and therefore is not sensitive to the chemical properties, but only to the potential, of the liquid being tested.

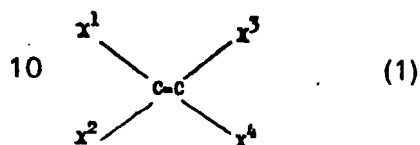
The polymer constituting the hydrophobic organic polymer used in this invention can be any polymer of a carbon-containing compound having a film-forming molecular weight corresponding to a degree of polymerization of at least 100: the type of carbon-containing polymer and the upper limit of the degree of polymerization are not critical. Cross-linkages may be introduced

into the polymeric membrane coating.

Polymers formed by polymerizing a monoolefin, halogenoethylene, conjugated diene or halogenated conjugated diene are preferred.

- 5 As the monoolefin, there can be mentioned those having 2 to 5 carbon atoms, such as ethylene, propylene, butene and isobutene, and among them, ethylene is especially preferred. 5

The halogenoethylene is preferably a compound represented by the following general formula:



- 15 where each of X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup> and X<sup>4</sup> is hydrogen, chlorine or fluorine, provided that not all of X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup> and X<sup>4</sup> stand for hydrogen. Examples are vinyl chloride, vinylidene chloride, vinyl fluoride, 15 trifluoroethylene, tetrafluoroethylene and tetrachloroethylene.

The conjugated diene or halogenated conjugated diene is preferably a compound represented by the following general formula:



where each of Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, Y<sup>4</sup>, Y<sup>5</sup> and Y<sup>6</sup> is a hydrogen atom, a chlorine atom, a fluorine atom or a C<sub>1-3</sub> alkyl group. Examples are butadiene, chloroprene, isoprene and hexachlorobutadiene.

- 30 Among these compounds, butadiene and hexachlorobutadiene are especially preferred. 30

Either homopolymers of the foregoing monomers or copolymers obtained by polymerizing at least two of the foregoing monomers can be used in this invention. From the viewpoint of the stability of the potential, it is preferred to use, from among the above-mentioned polymers, a homopolymer of trifluoroethylene, a homopolymer of tetrafluoroethylene, a trifluoroethylene-tetrafluoroethylene copolymer, a homopolymer of vinyl chloride, a homopolymer of vinylidene chloride or a copolymer of vinyl chloride and vinylidene chloride. The reason is that such halogen-containing polymers can easily be formed into a thin membrane and the resulting membrane has a high polarity.

- 35 35
- 40 Another type of hydrophobic organic polymer that can be used in this invention is a polysiloxane represented by the following general formula: 40



- 50 where each of Z<sup>1</sup> and Z<sup>2</sup> is an alkyl or aryl group having 1 to 10 carbon atoms in which one or more of the carbon atoms has a substituent such as a chlorine or bromine atom or a cyano group, and n is at least 100. Since these polysiloxanes have very high hydrophobic characteristics, they are preferably used. As such polysiloxanes, there can be mentioned, for example, polydimethylsiloxane, polyphenylsiloxane, polydecylsiloxane, polytrimethylsiloxane, polychlorophenylsiloxane, polymethylphenylsiloxane and polycyanoethylsiloxane. Among these siloxanes, 55 polydimethylsiloxane and polydiphenylsiloxane are preferred. In the above general formula, Z<sup>1</sup> and Z<sup>2</sup> may be the same as or different from one another. Further, not only homopolymers but also copolymers, such as copolymers including dimethylsiloxane units and diphenylsiloxane units and block copolymers thereof, can be used. Further, these polysiloxanes may be used in the form of block copolymers with other hydrophobic polymers, such as polycarbonates. 55

- 60 In order to improve the chemical resistance and mechanical strength in the resulting membrane, it is preferred that at the step of applying such a polysiloxane to the gate surface, a cross-linking agent such as an alkoxysilane, a hydroxysilane, an oxime silane or an acetoxysilane be incorporated into the polysiloxane and the cross-linking treatment carried out after the coating step. 60

zene, acrylonitrile, acrolein, vinyl acetate, methyl methacrylate, butyl acrylate, vinylidene cyanide, chlorostyrene and chloromethylstyrene may be used as the starting compound for formation of a hydrophobic polymer membrane for use in accordance with this invention.

In this invention, polymers derived from the above-mentioned various monomers can be used as membrane-forming materials, but polymers composed of monomers having dissociative groups such as carboxyl, amino and hydroxyl groups cannot be used because they are hydrophilic and have a degree of water content exceeding 0.5%.

It is essential that the polymer membrane that is used in this invention should not have pinholes, which have a bad influence on the electrode stability. It is preferred that the membrane be as thin as possible, so far as pinholes are avoided. When the thickness is large, an induced current having an influence on measured values is generated. So, the stability to the output change is gradually degraded with the increase of the thickness. The thickness of the membrane is ordinarily 500 Å to 1 μ and preferably 1000 to 3000 Å.

In this invention, it is preferred that the surface of the gate region be treated with a silane coupling agent prior to formation of the polymeric membrane. If the polymeric membrane is formed without giving this silanation treatment, dipping the coated FET into an aqueous solution for a long time will cause water to intrude between the gate surface of the FET and the polymeric membrane, and the FET becomes ion-sensitive. As the silane coupling agent, there can be mentioned compounds represented by the formula  $\text{CH}_2 = \text{CHSi}(\text{OR})_3$  or  $\text{CH}_2 = \text{C}(\text{CH}_3)\text{COOCH}_2\text{CH}_2\text{CH}_2\text{Si}(\text{OR})_3$  in which R stands for an alkyl group having 1 to 3 carbon atoms. The silanation treatment may be carried out according to a conventional method.

The polymeric membrane can be formed on the surface of the gate region by a number of methods, for example, (i) dissolving a hydrophobic organic polymer in an appropriate solvent, coating the resulting solution on the surface of the gate region and evaporating off the solvent; (ii) applying a monomer capable of forming a hydrophobic organic polymer or a monomer solution containing a partially polymerized product to the surface of the gate region and causing polymerization to proceed on the surface of the gate region to form a polymeric membrane.

In the method (i), the polymer can be obtained by polymerizing the monomer according to any known polymerization methods. The polymerization conditions are not particularly critical. In order to improve the film-forming property, the dielectric property and the electric conductivity of the polymer, additives such as non-ionic plasticizers and carbon may be incorporated into the membrane-constituting polymer. Especially when polyvinyl chloride is used, by incorporating 100 to 400 parts by weight of a plasticizer such as dioctyl phthalate, dioctyl adipate or tricresyl phosphate into 100 parts by weight of polyvinyl chloride, the film-forming property can be remarkably improved, and in this case a stable thin film can be formed on the surface of the gate region. It is preferred that the coating of the polymer solution on the surface of the gate region be carried out several times and the solvent be slowly evaporated after the coating operation.

In method (ii), it is preferred that the polymeric membrane be formed by plasma polymerization, ultraviolet polymerization or radiation polymerization. Such polymerization can be accomplished according to conventional polymerization techniques, and such conditions as the vapour pressure of the monomers, the polymerization temperature, the polymerization time and the dose of plasma, ultraviolet rays or actinic rays can be appropriately chosen.

In this invention, it is essential that the polymeric membrane should be formed at least on the gate region. It is preferred that the entire surface of the FET be coated with the polymeric membrane, because the coating process is simpler and there is no risk of insulation breakdown.

In measuring chemical properties by using the reference electrode of this invention, it is necessary to use a unit for measuring chemical properties in combination with a pseudo reference electrode.

Since the reference electrode is an insulated gate electrode, it is necessary to use independently a pseudo reference electrode to apply bias, and by the use of the pseudo reference electrode, the potential of an electrolyte solution is fixed and the difference of the output potential between the measuring unit and the reference electrode is detected based on the fixed potential of the electrode solution. For this detection, there is used a differential amplifier. In this case, the potential  $E_0$  of the pseudo reference electrode is the in-phase input voltage of the differential amplifier and has no influence on the output voltage  $V_0$  of the differential amplifier. In other words, the following relation is established:

$$\text{Output voltage} \propto \frac{[\text{ion sensor output } E_1 - E_0]}{[\text{reference electrode output } (E_R - E_0)]} = E_1 - E_R$$

Accordingly, any conductor can be used for the pseudo reference electrode. For example, an appropriate metal such as gold, silver or platinum or graphite may be used. The shape of the pseudo reference electrode is not particularly critical, provided it is constructed so that the

electrode is allowed to come into contact with the liquid being tested. Although the potential should be stable in the reference electrode, it need not be in the pseudo reference electrode, which can therefore be easily manufactured. For example, if a support of the FET sensor described hereinafter is formed of a metal, this support acts as a pseudo reference electrode.

5 The unit for measuring chemical properties, which is used in combination with the reference electrode of this invention, comprises an insulated-gate FET sensitive to chemical properties in the liquid to be tested. An FET as disclosed in the above-mentioned prior-art references can be used in accordance with this invention. The above-mentioned insulated-gate FET having a gate-insulating layer of a double-layer structure comprising a silicon dioxide layer and a silicon nitride  
10 layer is a preferred pH sensor, and an insulated-gate FET sensor having a membrane selectively sensitive to a specific chemical substance, e.g. of the type used for a glass electrode or the like, on the surface of a gate region of an ordinary FET, can be used for measuring various chemical properties described hereinbefore, especially the concentration and activity of ions in electro-  
lytes, according to the characteristics of the membrane.

15 An example of a membrane having a selective sensitivity is an inorganic membrane of an alkali metal silicate glass or an organic membrane containing a ligand to a specific substance. As the former silicate glass, there can be mentioned, for example, a glass of  $\text{SiO}_2 + \text{CaO} + \text{Na}_2\text{O}$  (72.2:6.4:21.4 molar ratio) which can be used for detection and measurement of pH and  $\text{pNa}^+$ . As the ligand to a specific substance, which is included in the latter membrane, there can  
20 be mentioned, for example, antibiotics such as Valinomycin and Nonactin and cyclic ligands such as crown ether and cryptant. As the membrane-constituting material, there can be mentioned, for example, polyvinyl chloride, celluloses, polyurethane and polystyrene, which may contain a plasticizer. Such a ligand-containing membrane is effective for detecting and measuring such metals as sodium, potassium, calcium and barium. Other examples of a  
25 membrane selectively sensitive to specific chemical substances are an antibody membrane, a hem membrane and a silver halide membrane. Antigens, oxygen gas and halogens can be detected and measured by these membranes, respectively. Further, various membranes disclosed in U.S. Patent No. 4,020,830 can be used in accordance with this invention, so can a multisensor having a selective sensitivity to different chemical substances. The multi-sensor may  
30 be plural FETs which are formed on a single silicon chip.

Illustrative embodiments of the present invention are shown by way of example in the accompanying drawings, in which

*Figures 1-a and 1-b* illustrate one embodiment of the reference electrode of this invention;

*Figure 2* is a plan view showing one embodiment of a pH measuring system comprising a pH  
35 sensor, a reference electrode and a pseudo reference electrode, which are formed on one silicon wafer;

*Figure 3* is a view showing the section taken along the line A-A in the pH measuring system shown in *Fig. 2*;

*Figure 4* is a diagram illustrating one embodiment of an electric circuit including the pH  
40 measuring system shown in *Fig. 2*;

*Figure 5* is a diagram illustrating the relation of the output difference in source voltages of the pH sensor and reference electrode to the pH value in the circuit shown in *Fig. 4*; and

*Figure 6* is a diagram illustrating a circuit for measuring the ion activity in an electrolyte solution.

45 *Figures 1-a and 1-b* illustrate the gate region of one embodiment of a reference electrode of this invention, which comprises an insulated gate FET having the gate region coated with a hydrophobic organic membrane. In the drawing, reference numeral 1 represents a  $p$ -type silicon substrate, and reference numerals 2 and 3 represent  $n$ -type diffusion layers of source and drain, respectively. Reference numeral 4 represents a channel, and reference numerals 5 and 6  
50 represent a terminal of source and drain, respectively. Reference numerals 7 and 8 represent a silicon nitride layer and a silicon oxide layer, respectively. These layers 7 and 8 have a thickness of 1000 Å and constitute a gate-insulating layer. A polyvinyl chloride membrane 9 having a thickness of 1000 Å is formed on the gate-insulating layer.

An embodiment of the measurement system of this invention, comprising a chemical property  
55 measuring unit, a pseudo reference electrode and a reference electrode, will now be described with reference to *Figs. 2 to 4*.

*Fig. 2* is a plan view illustrating an integrated measurement system comprising an FET sensor, a pseudo reference electrode and a reference electrode, each of which is formed on one silicon  
60 wafer 10. Reference numerals 11, 12 and 13 represent  $n$ -type silicon grooves formed on  $p$ -type silicon. More specifically, reference numeral 11 represents a common drain, reference numeral 12 represents a source of the reference electrode and reference numeral 13 represents a source of the sensor. Reference numeral 14 represents a pseudo reference electrode necessary for maintaining the potential of a liquid to be tested at a constant level, which is formed by vacuum deposition of gold. Reference numerals 15, 16, 17, 18 and 19 represent electrode portions of

substrate, respectively. Reference numerals 20 and 21 represent gate regions of the reference electrode and sensor, respectively. Fig. 3 is a view showing the section taken along the line A-A in Fig. 2, in which reference numerals 20, 21 and 22 represent the gate region of the reference electrode, the gate region of the sensor and the pseudo reference electrode, respectively. In the gate regions of the sensor and reference electrode, an ion-sensitive membrane 26 and a hydrophobic organic membrane 25 are coated, respectively, on a two-layer structure of silicon dioxide 24 and silicon nitride 23. If a two-layer structure of silicon dioxide 24 and silicon nitride 23 is formed on the gate region of the sensor, the system can be used as a pH sensor. Such sensor can be manufactured by a customary IC manufacturing technique according to a known method disclosed in, for example, published Japanese Patent Application No. 96890/78.

This integrated ion sensor system can be manufactured according to the following procedures.

At first, two electrodes 20 and 21 are formed on one silicon wafer. The surface of these regions is formed of a silicon nitride layer, and a gold electrode 14 is formed as a pseudo reference electrode by vacuum deposition of gold. Since the stability of the electrode potential and the like are of no particular significance in this pseudo reference electrode, an appropriate material capable of facilitating the integration operation can be used for this electrode. When the pseudo reference electrode is formed of gold, an undercoating of chromium having a thickness of about 1000 Å is formed by vacuum deposition and a gold layer having a thickness of about 1000 Å is formed thereon by vacuum deposition. When chromium is thus used, the adhesion of the gold electrode to the substrate can be improved.

Then, polyvinyl chloride is coated in a thickness of about 1000 Å on the gold electrode. The polyvinyl chloride membrane is left only in the area of the reference electrode 21 and in another area, the polyvinyl chloride membrane is removed. More specifically, aluminium is vacuum-deposited in a thickness of about 1000 Å in the area of the reference electrode, and by using the so-formed aluminium layer as a mask, the polyvinyl chloride membrane is removed from the area of the pH sensor 10 and the area of the gold electrode 14 by etching in oxygen plasma generated by a high-frequency wave of 13 MHz (the frequency is not particularly critical) under an oxygen pressure of about 0.5 torr. Then, the aluminium layer used as the mask for etching the polyvinyl chloride layer is removed, e.g. by a phosphoric acid etching solution. Thus, an integrated measurement system as shown in Fig. 2 is manufactured.

This measurement system comprises a sensor, a reference electrode and a pseudo reference electrode, each of which is formed on one silicon wafer. When these members are thus formed on one silicon wafer, a measurement system having a very small size can be prepared very easily. Therefore, this system can be said to be a particularly preferred embodiment of the measurement system of this invention. Of course, there may be adopted a method in which the foregoing three elements are separately prepared, or a method in which two of the foregoing three elements are formed on one silicon wafer.

Fig. 4 is a view illustrating diagrammatically an instance of the measuring circuit including the system illustrated in Fig. 2. Referring to Fig. 4, the measurement system is put in a liquid 28 to be tested, which is contained in a vessel 27. A constant voltage power source 31 is a common power source for a sensor 33 and a reference electrode 32, which is used for actuating the reference electrode and sensor in the saturation region. Reference numerals 35 and 36 represent constant current devices for maintaining constant electric currents for FET 32 and FET 33. Reference numeral 34 represents a pseudo reference electrode for maintaining the potential of the liquid to be tested at a constant level. The source voltages (outputs) of the sensor and reference electrode are amplified by impedance conversion circuits 37 and 38, respectively, and the output difference is detected by a subtracting circuit 39. This output difference is an output  $\Delta V$ s corresponding to the measured ion concentration, etc.

By using the reference electrode of this invention, the size of the measurement system can be decreased and especially when this reference electrode and a chemical-property-measuring unit including an insulated-gate FET are formed on one silicon wafer, there can be obtained an integrated measurement system having a much diminished size. If such a measurement system is used, the activity of specific ions can be measured without the effect of electric potential (for example, action/potential of a living body) in an electrolyte solution. This feature provides characteristic advantages when the measurement system is used as an ion sensor for a living body. In the case of a conventional ion sensor not using the reference electrode of this invention, changes of the electric potential in an electrolyte solution would generate noises for the output of the ion sensor.

Embodiments of this invention will now be described in detail by reference to the following illustrative examples.

#### Example 1

A solution of 5 mg of polyvinyl chloride (Geon 400X150P manufactured by Japanese Geon Co., Ltd.) and 5 mg of dioctyl phthalate in 150 ml of tetrahydrofuran was coated on the gate region of an FET having a two-layer structure of silicon dioxide and silicon nitride (disclosed in

published Japanese Patent Application No. 96890/78) and the coating was dried to form the reference electrode. A circuit as shown in Fig. 4 was constructed by using the thus-formed reference electrode in combination with the above FET, which was not subjected to the above coating treatment, as a pH sensor. The relation between the pH and the output difference  $\Delta V$ s in the source voltages of the FET sensor and the reference electrode, which was observed in the thus-constructed circuit, is shown in Fig. 5. In this experiment, a silver wire was used as the pseudo reference electrode and the measurement was carried out at a drain voltage of 1.5 V and a drain current of 30  $\mu$ A. A pH buffer solution described in Japanese Industrial Standard (JIS) 28802-1954 was used as the buffer solution and human blood was used as a liquid to be tested.

From the results shown in Fig. 5, it can readily be understood that a good linear relation is established between the pH and  $\Delta V$ s irrespectively of the kind and concentration of ions. Thus, it has been confirmed that an FET coated with a polyvinyl chloride membrane can be satisfactorily used as a reference electrode.

#### Example 2

A membrane of a polymeric substance indicated in Table 1 was formed on the gate region of the same FET as used in Example 1 by the following coating procedures.

First, a polymer solution having a concentration indicated in the Table below was prepared and the gate region of FET was dipped in the solution. The dipped FET was sufficiently shaken to remove the excess of solution, and the solvent was removed by drying.

In order to check whether the so formed electrode could be used as a reference electrode, the pH sensitivity of the electrode was determined according to the following method, and when the pH sensitivity was lower than 5 mV/pH, it was judged that the electrode could be used as a reference electrode.

#### pH Determination Method:

The formed electrode was used as a pH sensor and a calomel electrode was used as a reference electrode. The pH buffer solution described in Example 1 was used as the liquid to be tested. The measurement circuit used is shown in Fig. 6, in which reference numeral 40 represents the pH sensor, reference numeral 41 represents the reference electrode for maintaining the potential of the liquid to be tested at a certain level, and reference numeral 42 represents a voltage meter indicating the surface potential of the gate-insulating layer. On the pH sensor side, there was used a source follower circuit of a low output resistance including a resistance 44 connected to the source, and the output of this circuit was displayed on the voltage meter. The source voltage was measured under conditions of a drain current of 30  $\mu$ A and a drain voltage of 5 V.

The results thus obtained are shown in the Table below. From these results, the following can be seen.

When the electrode is coated with a hydrophobic polymer having a degree of water content lower than 0.5% as in runs nos. 1 and 2, the sensitivity to the pH is apparently low. Accordingly, it is seen that an electrode coated with a hydrophobic membrane can be used as a reference electrode.

In contrast, when an electrode is coated with a hydrophilic membrane having a high degree of water content, the sensitivity to the pH is very high and this electrode cannot be used as a reference electrode.

Incidentally, when the polymer solutions of runs nos. 1 and 2 were separately coated on glass sheets in the same manner, the thickness of the formed membrane was 2000 Å in case of the polymer solution of run No. 1 and 3000 Å in case of the polymer solution of run No. 2.



Table 1

Run No.	Polymer (degree of water content, %)	Polymer Solution		Source Voltage			
		Solvent	C'	pH 4	pH 7	pH 9	
1	polydimethylsiloxane <sup>a</sup> (0.0)	dimethyl ether	0.5	1.194	- 1.195	- 1.196	5
2	copolymer of vinyl chloride and vinylidene chloride (0.3)	tetrahydrofuran	2	1.442	1.446	1.433	10
3	polyvinyl alcohol <sup>c</sup> (water-soluble)	water	0.5	0.682	0.515	0.396	
4	polyhydroxyethyl methacrylate <sup>d</sup> (60)	95% ethanol	2	1.156	1.005	0.897	15
5	copolymer of hydroxyethyl methacrylate and methyl methacrylate	acetone	1	0.326	0.188	0.090	
6	untreated			1.165	1.007	0.884	20

## Note

- (a) Silicone KE44 manufactured by Shinetsu Kagaku Kogyo Co. Ltd.
- (b) copolymer of vinyl chloride and vinylidene chloride (5:95 molar ratio) obtained by solution polymerization using cyclohexanone as the solvent and azobisisobutyronitrile as the catalyst
- (c) Kuraray Poval 117 manufactured by Kuraray Co. Ltd.
- (d) polymer obtained by solution polymerization of hydroxyethyl methacrylate by using pure ethanol as the solvent and isopropyl percarbonate as the catalyst
- (e) copolymer of hydroxyethyl methacrylate and methyl methacrylate (20:80 molar ratio) obtained by solution polymerization using ethanol as the solvent and isopropyl percarbonate as the catalyst
- (f) concentration in weight per cent of polymer in solvent.

## Example 3

The surface of the gate region of the same FET as used in Example 1 was treated with a 5% aqueous solution of vinyl- $\beta$ -methoxyethoxysilane and a hydrophobic membrane was prepared on the surface of the gate region by ultraviolet polymerization according to the following procedures.

- The surface-treated FET was placed in a quartz tube and the interior of the tube was evacuated to  $10^{-3}$  mm Hg using a vacuum line. Then, vinylidene chloride at a pressure of 80 mm Hg and vinyl chloride at a pressure of 20 mm Hg were introduced into the interior of the tube. The tube was exposed to rays from 1 KW xenon lamp for 4 hours to effect ultraviolet polymerization on the surface of the gate region of FET and to form a membrane of vinyl-chloride:vinylidene-chloride copolymer. The coated FET was taken out from the quartz tube and aging was carried out overnight at 80°C.

The pH sensitivity of the thus-prepared electrode was examined according to the method described in Example 2. As a result, it was found that the change of the source potential according to the pH change was as low as 2 mV/pH. Thus, it has been confirmed that the thus-prepared hydrophobic-membrane-coated electrode can be used as a reference electrode. Further, it was observed that even after 24 hours' dipping in water, this electrode was stable.

## CLAIMS

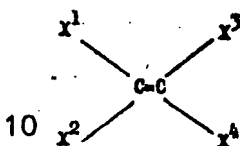
1. A reference electrode comprising an insulated gate field effect transistor in which the surface of the gate region is coated with a hydrophobic and non-ionic organic polymeric membrane.
2. An electrode as claimed in Claim 1 in which the organic polymer of which the membrane is composed is obtained by polymerizing at least one monoolefin, halogenoethylene, conjugated diene and/or halogenated conjugated diene.
3. An electrode as claimed in Claim 2 in which the organic polymer is obtained by polymerizing one monoolefin, haloenoethylene, conjugated diene or halogenated conjugated diene.
4. An electrode as claimed in Claim 2 in which the organic polymer is obtained by polymerizing at least two of the said monomers.
5. An electrode as claimed in Claim 2, 3 or 4 in which the monoolefin is a monoolefin

having 2 to 5 carbon atoms in the molecule.

6. An electrode as claimed in Claim 5 in which the monoolefin is ethylene.

7. An electrode as claimed in Claim 2, 3 or 4 in which the halogenoethylene is a compound represented by the following general formula:

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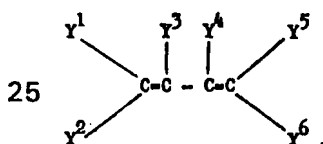
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where each of  $X^1$ ,  $X^2$ ,  $X^3$  and  $X^4$  is hydrogen, chlorine or fluorine, provided that not all of  $X_1$ ,  $X_2$ ,  $X_3$  and  $X_4$  stand for hydrogen.

15 8. An electrode as claimed in Claim 7 in which the halogenoethylene is trifluoroethylene or tetrafluoroethylene. 15

9. An electrode as claimed in Claim 7 in which the halogenoethylene is vinyl chloride or vinylidene chloride.

10. An electrode as claimed in Claim 2, 3 or 4 in which the conjugated diene or 20 halogenated conjugated diene is a compound represented by the following general formula: 20



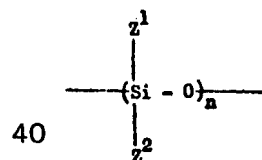
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where each of  $Y^1$ ,  $Y^2$ ,  $Y^3$ ,  $Y^4$ ,  $Y^5$  and  $Y^6$  is a hydrogen atom, a chlorine atom, a fluorine atom or 30 a  $C_{1-3}$  alkyl group. 30

11. An electrode as claimed in Claim 10 in which the conjugated diene or halogenated conjugated diene is butadiene or hexachlorobutadiene.

12. An electrode as claimed in Claim 1 in which the hydrophobic organic polymeric membrane is a membrane of a polysiloxane represented by the following general formula:

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where each of  $Z^1$  and  $Z^2$  is an alkyl or aryl group having 1 to 10 carbon atoms in which one or 45 more of the carbon atoms has a substituent such as a chlorine or bromine atom or a cyano group, and  $n$  is at least 100. 45

13. An electrode as claimed in Claim 12 in which the polysiloxane is polydimethylsiloxane or polydiphenylsiloxane.

14. An electrode as claimed in any one of Claims 1 to 13 in which the thickness of the hydrophobic organic polymeric membrane is 500 to 10,000 Å.

15. A system for measuring chemical properties comprising a chemical-property-measuring 50 unit including an insulated gate field effect transistor that is sensitive to chemical properties in a liquid to be tested; a reference electrode comprising an insulated-gate field-effect transistor, the surface of the gate region of which is coated with a hydrophobic organic polymeric membrane so that the transistor is not sensitive to chemical properties in the liquid to be tested; and a 55 pseudo reference electrode comprising an electrode formed of a good electric conductor. 55

16. A measuring system as claimed in Claim 15 in which the chemical-property-measuring unit is so arranged that an electrolyte is caused to have direct contact with a gate-insulating layer of the insulated-gate field-effect transistor to determine pH or pNa.

17. A measuring system as claimed in Claim 15 in which the chemical-property-measuring 60 unit is one in which an organic polymeric membrane containing a ligand capable of selectively adsorbing a specific chemical substance is formed on a gate-insulating layer of the insulated-gate field-effect transistor so that the transistor is sensitive to the said specific chemical substance. 60

18. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric

19. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 3.
20. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 4.
- 5 21. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 5. 5
22. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 6.
23. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 7. 10
- 10 24. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 8. 10
25. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 9.
- 15 26. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 10. 15
27. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 11.
28. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 12. 20
- 20 29. A measuring system as claimed in Claim 15, 16 or 17 in which the organic polymeric membrane is as defined in Claim 13.
30. A measuring system as claimed in Claims 15 to 29 in which the thickness of the hydrophobic organic polymeric membrane is 500 to 10,000 Å.
- 25 31. A measuring system as claimed in any one of Claims 15 to 30 in which the chemical property measuring units, the reference electrode and the pseudo reference electrode are formed on one silicon wafer. 25
32. A reference electrode substantially as hereinbefore described with reference to Figs. 1a and 1b of the accompanying drawings.
- 30 33. A measuring system substantially as hereinbefore described with reference to Figs. 2 and 3 of the accompanying drawings. 30
34. An electrode as claimed in Claim 1 obtained by a method substantially as hereinbefore described in Example 1, 2 or 3.